

Amendments to the Specification:

Please cancel the Abstract filed with the application and substitute with the replacement Abstract, that is in compliance with 37 C.F.R. § 1.72, submitted herewith as a separate sheet.

Please amend the paragraph starting at page 171, line 35 as follows:

56. Full-length PRO701 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO701. In particular, Applicants have identified and isolated cDNA encoding a PRO701 polypeptide, as disclosed in further details in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO701 polypeptide have significant homology with the neuroligins 1, 2 and 3 and esterases including carboxyesterases and ~~acetylcholinesterases~~ acetylcholinesterases. Accordingly, it is presently believed that the PRO701 polypeptide disclosed in the present application is a newly identified member of the neuroligin family and is involved in mediating recognition processes between neurons and/or functions as a cell adhesion molecule as is typical of neuroligins.

Please amend the paragraph beginning at page 124, line 27, as follows:

Percent amino acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). ~~The NCBI-BLAST2 sequence comparison program may be downloaded from~~ <http://www.ncbi.nlm.nih.gov>. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

Please amend the paragraph beginning at page 127, line 10, as follows:

Percent nucleic acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). ~~The NCBI-BLAST2 sequence comparison program may be downloaded from~~

~~http://www.ncbi.nlm.nih.gov~~ NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

Please amend the paragraph beginning at page 237, line 2, as follows:

A cDNA sequence isolated in the amylase screen as described in Example 2 above was found, by BLAST and FastA sequence alignment, to have sequence homology to a nucleotide sequence encoding sarcoma-associated protein SAS. This cDNA sequence is herein designated DNA23020 (see Figure 16). The DNA23020 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQTM, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington; ~~http://bozeman.mbt.washington.edu/phrap/docs/phrap.html~~). The consensus sequence obtained therefrom is herein designated DNA35858. Two proprietary Genentech ESTs were employed in the assembly wherein those EST sequences are herein identified as DNA21971 (Figure 17; SEQ ID NO:38) and DNA29037 (Figure 18; SEQ ID NO:39).

Please amend the paragraph beginning at page 278, line 26, as follows:

A cDNA sequence was isolated in the amylase screen described in Example 2 above and is herein designated DNA13199 (Figure 134; SEQ ID NO:332). The DNA13199 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into

consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington; ~~http://bozeman.mbt.washington.edu/phrap.does/phrap.html~~). The consensus sequence obtained therefrom is herein designated as DNA22778.

Please amend the paragraph beginning at page 279, line 26, as follows:

A cDNA sequence isolated in the amylase screen described in Example 2 above was herein designated DNA37642 (Figure 137, SEQ ID NO:338). The DNA37642 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologies therebetween. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington; ~~http://bozeman.mbt.washington.edu/phrap.does/phrap.html~~). The consensus sequence obtained is herein designated DNA48615.

Please amend the paragraph beginning at page 313, line 27, as follows:

A cDNA isolated in the amylase screen described in Example 2 above is herein designated DNA26832 (Figure 220; SEQ ID NO:516). The sequence of DNA26832 was then used to search expressed sequence tag (EST) databases. The EST databases included public EST databases (e.g., GenBank) and a proprietary EST database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266: 469-480 [1996]). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, ~~Washington~~; ~~http://bozeman.mbt.washington.edu/phrap.does/phrap.html~~).

Please amend the paragraph beginning at page 315, line 20, as follows:

Human thrombopoietin (THPO) is a glycosylated hormone of 352 amino acids consisting of two domains. The N-terminal domain, sharing 50% similarity to erythropoietin, is responsible

for the biological activity. The C-terminal region is required for secretion. The gene for thrombopoietin (THPO) maps to human chromosome 3q27-q28 where the six exons of this gene span 7 kilobase base pairs of genomic DNA (Chang et al., Genomics 26: 636-7 (1995); Foster et al., Proc. Natl. Acad. Sci. USA 91: 13023-7 (1994); Gurney et al., Blood 85: 981-988 (1995). In order to determine whether there were any genes encoding THPO homologues located in close proximity to THPO, genomic DNA fragments from this region were identified and sequenced. Three P1 clones and one PAC clones (Genome Systems Inc., St. Louis, MO; cat. Nos. P1-2535 and PAC-6539) encompassing the THPO locus were isolated and a 140 kb region was sequenced using the ordered shotgun strategy (Chen et al., Genomics 17: 651-656 (1993)), coupled with a PCR-based gap filling approach. Analysis reveals that the region is gene-rich with four additional genes located very close to THPO: tumor necrosis factor-receptor type 1 associated protein 2 (TRAP2) and elongation initiation factor gamma (~~eIF4~~) (eIF4g), chloride channel 2 (CLCN2) and RNA polymerase II subunit hRPB17. While no THPO homolog was found in the region, four novel genes have been predicted by computer-assisted gene detection (GRAIL)(Xu et al., Gen. Engin. 16: 241-253 (1994), the presence of CpG islands (Cross, S. and Bird, A., Curr. Opin. Genet. & Devel. 5: 109-314 (1995), and homology to known genes (as detected by WU-BLAST2.0)(Altschul and Gish, Methods Enzymol. 266: 460-480 (1996) (<http://blast.wustl.edu/blast/README.html>).

Please amend the paragraph beginning at page 317, line 1, as follows:

ABI DYE-primerTM chemistry (PE Applied Biosystems, Foster City, CA; Cat. No.: 402112) was used to end-sequence the lambda and plasmid subclones. ABI DYE-terminatorTM chemistry (PE Applied Biosystems, Foster City, CA, Cat. No: 403044) was used to sequence the PCR products with their respective PCR primers. The sequences were collected with an ABI377 instrument. For PCR products larger than 1kb, walking primers were used. The sequences of contigs generated by the OSS strategy in AutoAssemblerTM (PE Applied Biosystems, Foster City, CA; Cat. No: 903227) and the gap-filling sequencing trace files were imported into SequencerTM (Gene Codes Corp., Ann Arbor, MI) for overlapping and editing. The sequences generated by the total shotgun strategy were assembled using Phred and Phrap and edited using Consed (<http://chimera.biotech.washington.edu/uwgc/projects.htm>) and GFP (Genome Reconstruction Manager for Phrap), version 1.2 (<http://stork.cellb.bcm.tmc.edu/gfp/>).

Please amend the paragraph beginning at page 317, line 21, as follows:

The identification and characterization of coding regions was carried out as follows:

First, repetitive sequences were masked using RepeatMasker (A.F.A. Smit & P. Green; http://ftp.genome.washington.edu/RM/RM_details.html) which screens DNA sequences in FastA format against a library of repetitive elements and returns a masked query sequence. Repeats not masked were identified by comparing the sequence to the GenBank database using WUBLAST2.0 [Altschul, S & Gish, W., Methods Enzymol. 266: 460-480 (1996); <http://blast.wustl.edu/blast/README.html>] and were masked manually.

Please amend the paragraph beginning at page 376, line 34, as follows:

The following materials have been deposited with the American Type Culture Collection, [12301 Parklawn Drive, Rockville, MD,] 10801 University Boulevard, Manassas, VA 20110-2209, USA (ATCC):

<u>Material</u>	<u>ATCC Dep. No.</u>	<u>Deposit Date</u>
DNA39987-1184	ATCC 209786	April 21, 1998
DNA40625-1189	ATCC 209788	April 21, 1998
DNA23318-1211	ATCC 209787	April 21, 1998
DNA39979-1213	ATCC 209789	April 21, 1998
DNA40594-1233	ATCC 209617	February 5, 1998
DNA45416-1251	ATCC 209620	February 5, 1998
DNA45419-1252	ATCC 209616	February 5, 1998
DNA52594-1270	ATCC 209679	March 17, 1998
DNA45234-1277	ATCC 209654	March 5, 1998
DNA49624-1279	ATCC 209655	March 5, 1998
DNA48309-1280	ATCC 209656	March 5, 1998
DNA46776-1284	ATCC 209721	March 31, 1998
DNA50980-1286	ATCC 209717	March 31, 1998
DNA50913-1287	ATCC 209716	March 31, 1998
DNA50914-1289	ATCC 209722	March 31, 1998
DNA48296-1292	ATCC 209668	March 11, 1998
DNA32284-1307	ATCC 209670	March 11, 1998
DNA36343-1310	ATCC 209718	March 31, 1998
DNA40571-1315	ATCC 209784	April 21, 1998
DNA41386-1316	ATCC 209703	March 26, 1998
DNA44194-1317	ATCC 209808	April 28, 1998
DNA45415-1318	ATCC 209810	April 28, 1998
DNA44189-1322	ATCC 209699	March 26, 1998
DNA48304-1323	ATCC 209811	April 28, 1998
DNA49152-1324	ATCC 209813	April 28, 1998

DNA49646-1327	ATCC 209705	March 26, 1998
DNA49631-1328	ATCC 209806	April 28, 1998
DNA49645-1347	ATCC 209809	April 28, 1998
DNA45493-1349	ATCC 209805	April 28, 1998
DNA48227-1350	ATCC 209812	April 28, 1998
DNA41404-1352	ATCC 209844	May 6, 1998
DNA44196-1353	ATCC 209847	May 6, 1998
DNA52187-1354	ATCC 209845	May 6, 1998
DNA48328-1355	ATCC 209843	May 6, 1998
DNA56352-1358	ATCC 209846	May 6, 1998
DNA53971-1359	ATCC 209750	April 7, 1998
DNA50919-1361	ATCC 209848	May 6, 1998
DNA44179-1362	ATCC 209851	May 6, 1998
DNA54002-1367	ATCC 209754	April 7, 1998
DNA53906-1368	ATCC 209747	April 7, 1998
DNA52185-1370	ATCC 209861	May 14, 1998
DNA53977-1371	ATCC 209862	May 14, 1998
DNA57253-1382	ATCC 209867	May 14, 1998
DNA58847-1383	ATCC 209879	May 20, 1998
DNA58747-1384	ATCC 209868	May 14, 1998
DNA57689-1385	ATCC 209869	May 14, 1998
DNA23330-1390	ATCC 209775	April 14, 1998
DNA26847-1395	ATCC 209772	April 14, 1998
DNA53974-1401	ATCC 209774	April 14, 1998
DNA57039-1402	ATCC 209777	April 14, 1998
DNA57033-1403	ATCC 209905	May 27, 1998
DNA34353-1428	ATCC 209855	May 12, 1998
DNA45417-1432	ATCC 209910	May 27, 1998
DNA39523-1192	ATCC 209424	October 31, 1997
DNA44205-1285	ATCC 209720	March 31, 1998
DNA50911-1288	ATCC 209714	March 31, 1998
DNA48329-1290	ATCC 209785	April 21, 1998
DNA48306-1291	ATCC 209911	May 27, 1998
DNA48336-1309	ATCC 209669	March 11, 1998
DNA44184-1319	ATCC 209704	March 26, 1998
DNA48314-1320	ATCC 209702	March 26, 1998
DNA48333-1321	ATCC 209701	March 26, 1998
DNA50920-1325	ATCC 209700	March 26, 1998
DNA50988-1326	ATCC 209814	April 28, 1998
DNA48331-1329	ATCC 209715	March 31, 1998
DNA30867-1335	ATCC 209807	April 28, 1998
DNA55737-1345	ATCC 209753	April 7, 1998
DNA49829-1346	ATCC 209749	April 7, 1998
DNA52196-1348	ATCC 209748	April 7, 1998
DNA56965-1356	ATCC 209842	May 6, 1998
DNA56405-1357	ATCC 209849	May 6, 1998

DNA57530-1375	ATCC 209880	May 20, 1998
DNA56439-1376	ATCC 209864	May 14, 1998
DNA56409-1377	ATCC 209882	May 20, 1998
DNA56112-1379	ATCC 209883	May 20, 1998
DNA56045-1380	ATCC 209865	May 14, 1998
DNA59294-1381	ATCC 209866	May 14, 1998
DNA56433-1406	ATCC 209857	May 12, 1998
DNA53912-1457	ATCC 209870	May 14, 1998
DNA50921-1458	ATCC 209859	May 12, 1998
DNA29101-1122	ATCC 209653	March 5, 1998
DNA40021-1154	ATCC 209389	October 17, 1997
DNA42663-1154	ATCC 209386	October 17, 1997
DNA30943-1-1163-1	ATCC 209791	April 21, 1998
DNA64907-1163-1	ATCC 203242	September 9, 1998
DNA64908-1163-1	ATCC 203243	September 9, 1998
DNA39975-1210	ATCC 209783	April 21, 1998
DNA43316-1237	ATCC 209487	November 21, 1997
DNA55800-1263	ATCC 209680	March 17, 1998
DNA94832-2659	240-PTA	June 15, 1999
DNA52758-1399	ATCC 209773	April 14, 1998

Please amend the paragraph beginning at page 378, line 33, as follows:

These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations there under (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent, assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC § 122 and the Commissioner's rules pursuant thereto (including 37 CFR § 1.14 with particular reference to 886 OG 638).